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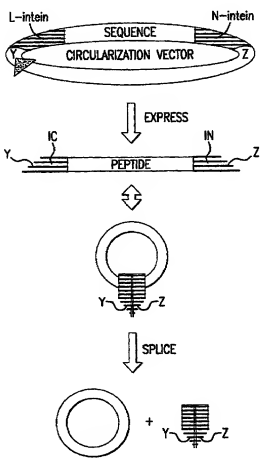
(54) Title: INTEIN-MEDIATED CYCLIZATION OF PEPTIDES



(57) Abstract: Methods of producing cyclic peptides and splicing intermediates of peptides in a looped conformation are disclosed. The methods utilize the trans-splicing ability of split inteins to catalyze cyclization of peptides from a precursor peptide having a target peptide interposed between two portions of a split intein. The interaction of the two portions of the split intein creates a catalytically-active intein and also forces the target peptide into a loop configuration that stabilizes the ester isomer of the amino acid at the junction between one of the intein portions and the target peptide. A heteroatom from the other intein portion then reacts with the ester to form a cyclic ester intermediate. The active intein catalyzes the formation of an aminosuccinimide that liberates a cyclized form of the target peptide, which spontaneously rearranges to form the thermodynamically favored backbone cyclic peptide product. Also disclosed are nucleic acid molecules, polypeptides, methods for making cyclic peptides, methods of making libraries, and methods of screening peptides.

WO 00/36093 A3